Review Article

A Systematic Review of Anemia among Adolescents Girls

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ABSTRACT

Anemia is currently one of the most common and intractable nutritional problem globally. In developing countries, the adolescent group is more exposed to nutritional challenges and adolescent girls are more vulnerable to the disease. Adolescent girls are particularly prone to iron deficiency anemia because of the increased demands of iron by the body. It is astonishing to know that 30% of world population suffers from iron deficiency anemia, of which 80 to 90% are in developing countries. In India the prevalence of anemia among adolescent girls is 56% and this amounts to an average 64 million girls at any point in time. Specific actions like encouraging consumption of iron rich foods though dietary change, nutritional education, treatment and prevention of parasitic infections, weekly iron supplementation etc. are implemented to prevent iron deficiency anemia and improve the iron status among adolescent girls, yet the impact of anemia among adolescent girls is still a public health problem.

Key words: Adolescent girls, Iron deficiency anemia, Nutritional education

INTRODUCTION

Anemia is currently one of the most common and intractable nutritional problems globally.[1] Anemia is defined as a condition in which the number of red blood cells and their oxygen carrying capacity is insufficient to meet the body's pathologic needs. It is a condition where in the number of red blood cells are < 4.2 million/ µl or haemoglobin level < 12g/dl in women and < 13g/dl in men.[2] Globally, anemia is most common nutritional problem affecting around 2 billion of the world's population and more than 89% of this burden occurs in developing countries.[3,4]

Anemia may develop at any stage of life cycle [6] but children, adolescent girls and women of reproductive age are at high risk for developing anemia. [5,6] Adolescent girls are particularly prone to iron deficiency anemia because of the increased demands of iron by the body, since adolescent period signalizes the beginning of menstrual period in girls.[7] In India, the prevalence of anemia among adolescent girls was 56% and this amounts to an average 64 million girls at any point in time. [8] There are many studies focused on anemia among pregnant women and children but only few studies are available on anemia among adolescent girls, hence this study was undertaken.[9]

Types of anemia : [10,11]

1. Nutritional deficiency anemias: The different types of Nutritional deficiency anemias are- A. Iron deficiency anemia, B. Vitamin B_{12} deficiency anemia, C. Folic Acid deficiency anemia

2. Anemia of chronic disease: Anemia of chronic disease is a common disorder associated with a wide variety of inflammatory diseases including- Arthritis, Malignancies and Inflammatory Bowel Disease.

3. Sideroblastic anemias: Sideroblastic anemias are a group of conditions that are diagnosed by finding ring sideroblasts in the bone marrow. They are both hereditary and acquired forms.

4. Megaloblastic anemias: The megaloblastic anemias are macrocytic anemias characterized by raised Mean Corpuscular Volume (MCV) and associated with an abnormality in the maturation of haematopoietic cells in the bone marrow. The two major causes are Folate deficiency and Vitamin B12 deficiency. Pernicious anemia is a specific autoimmune disease that causes malabsorption of Vitamin B12 due to lack of intrinsic factor.

5. Hemolytic anemias:Hemolytic anemia is caused due to the destruction of RBC. In the hemolytic anemias there is reduced lifespan of the erythrocytes. Hemolytic Anemia results if the rate of destruction of the erythrocytes exceeds the rate of production. There is a wide range of haemolytic anemias with both genetic and acquired disorders. Haemolytic anemias account for approximately 5% of all anemias.The types of Haemolytic anemias are- Autoimmune Haemolytic Anemia, Sickle Cell Anemia, Thalassaemia and Glucose-6-Phosphate Dehydrogenase deficiency Anemia.

Etiology of anemia: [10]

At a biological level, anemia develops because of an imbalance in erythrocyte loss relative to production; this can be due to ineffective or deficient erythropoiesis (e.g.from nutritional deficiencies, inflammation, or genetic Hemoglobin disorders) and/or excessive loss of erythrocytes (due to hemolysis, blood loss, or both).

Figure 1 is a conceptual model of the etiology of anemia identifying how distal factors contribute to more proximate determinants of anemia, such as food insecurity, clean water, and sanitation and ultimately, the most immediate causes of anemia (e.g., nutritional deficiencies, disease,

inflammation, and Hb disorders). Many of these determinants are interrelated. Poverty, for example, is a major determinant of health and nutrition and poor socioeconomic position is linked to a greater risk of anemia among women and children. Similarly, low education level is also associated with a greater risk of anemia.

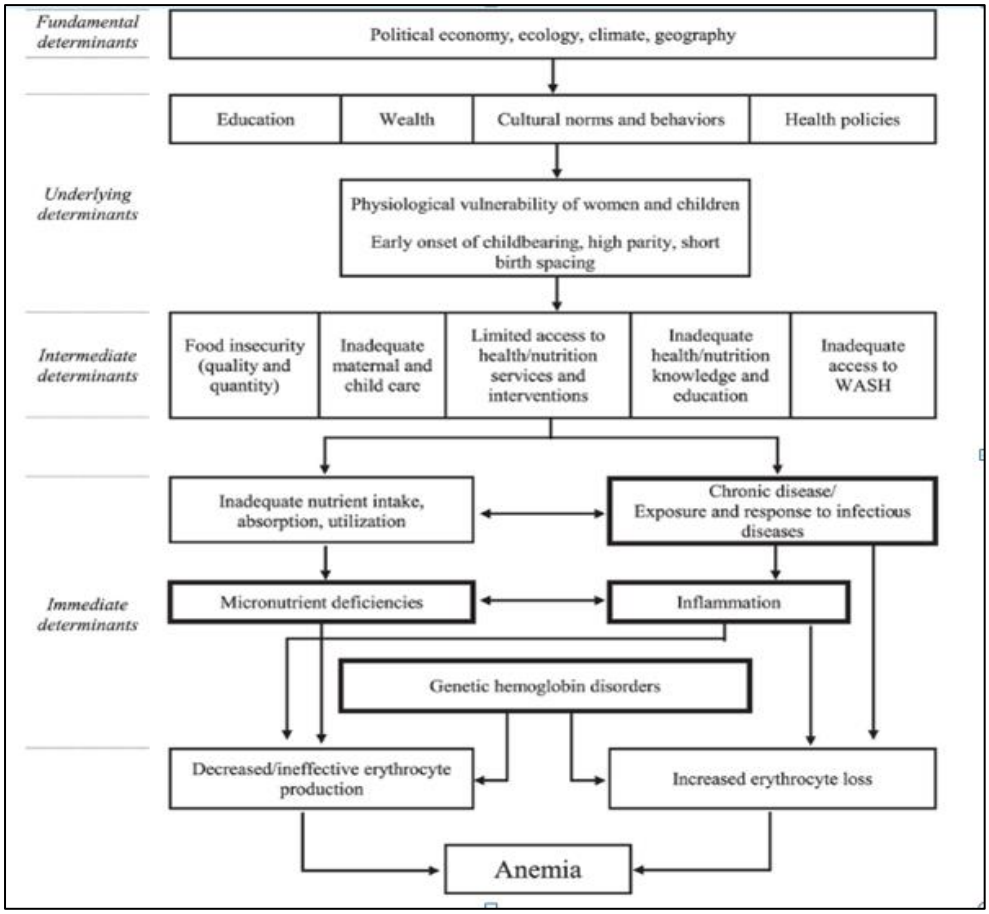

Figure 1 Etiology of Anemia

Pathophysiology of anemia:

The pathophysiology of anemia varies greatly depending on the primary cause. For instance, in acute hemorrhagic anemia, it is the restoration of blood volume with intracellular and extracellular fluid that dilutes the remaining red blood cells (RBCs), which results in anemia. A proportionate reduction in both plasma and red cells results in falsely normal hemoglobin and hematocrit. RBC are produced in the bone marrow and released into circulation. Approximately 1% of the RBC are removed from circulation per day. Imbalance in production to removal or destruction of RBC leads to anemia. [12] The main mechanisms involved in anemia are listed below:

1. **Increased RBC destruction**

A. Blood loss a. Acute- hemorrhage, surgery, trauma, menorrhagia b. Chronic- heavy menstrual bleeding, chronic gastrointestinal blood losses [13] (in the setting of hookworm infestation, ulcers, etc.), urinary losses (Benign Prostatic Hypertrophy, renal carcinoma, schistosomiasis)

B. Hemolytic anemia

Acquired- immune-mediated, infection, microangiopathic, blood transfusion-related, and secondary to hypersplenismo Hereditary- enzymopathies, disorders of hemoglobin (sickle cell), defects in red blood cell metabolism (G6PD deficiency, pyruvate kinase deficiency), defects in red blood cell membrane production (hereditary spherocytosis and elliptocytosis)

2**. Deficient/defective Erythropoiesis**

a. Microcytic- It is a condition in which the body's tissues and organs do not get enough oxygen.
b. Normocytic, normochromic- It is a condition in which the red blood cells are normal in size but lower in number.
c. Macrocytic -It is defined as blood with an insufficient concentration of haemoglobin.[14,15]

Clinical manifestations of Anemia: [11]

1. Mildest form: Lethargy and tiredness, reduced physical exercise, reduced mental performance and reduced tissue oxygenation causing dysfunction.
2. Severe form: rapid dysfunction, shock with collapse, dyspnoea, tachycardia and death

Diagnosis: [16]

1. **Hematologic Tests :**

a. Full blood screen
b. Hb concentretion
c. Cell count and mean corpuscular volume (MCV)
d. Hematocrit value(Hct), Mean Corpuscular Haemoglobin (MCH) and the Mean Corpuscular Haemoglobin Concentration (MCHC) are calculated automatically
e. Reticulocyte counts
f. White blood cell count
g. Platelet count
h. Microscopic examination of peripheral blood smears
i. Bone marrow aspirates

2. **Biochemical Tests:**

a. Measure serum iron vitamin concentrations (B12 and folate)
b. Measure levels of transport proteins (transferrin, Transcobalamin II)
c. Serum ferritin

1. Nutritional deficiency anemia:

A. Iron Deficiency Anemia : Iron deficiency occurs when the body's iron stores are insufficient for the normal formation of Hb, iron-containing enzymes, and other functional iron compounds such as myoglobin and those of the cytochrome system.[16,17]

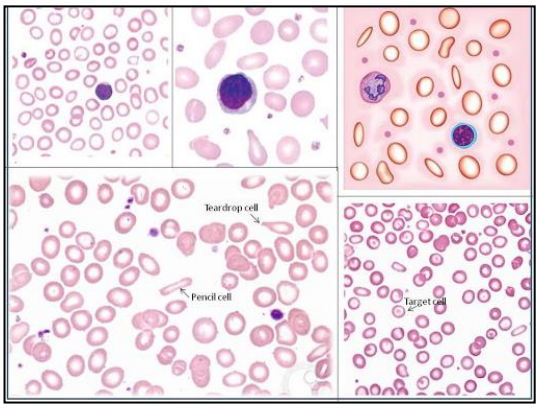

Figure 2: Iron deficiency Anemia

Most important risk factors determining iron deficiency anemia:[17]

1. An inadequate diet, with poor iron, micronutrient and vitamin content.
2. The use of medication and food that inhibit iron absorption including antacids, aspirin, nonsteroidal anti-inflammatory drugs, and excessive phytate, phosphate, oxalate and tannin intake.
3. Overweight and obesity.
4. Malabsorption syndrome.
5. Sports anemia seen in athletes.
6. Iron deficiency caused by blood loss resulting from Injury, accidents or blood donation.
7. Iron loss due to Parasitosis of the gastrointestinal tract (Entamoeba histolytica), Esophagitis, Atrophic gastritis, Colitis, Helicobacter pylori infection, Coeliac disease, Inflammatory Bowel Disease, Diverticulosis, Hemorrhoids, Gastrectomy or Gastroplasty (bariatric surgery), etc.
8. Genitourinary iron loss of various etiologies including Paroxysmal Nocturnal Hemoglobinuria and Glomerulonephritis.
9. Pregnancy, childbirth and the use of intrauterine devices.

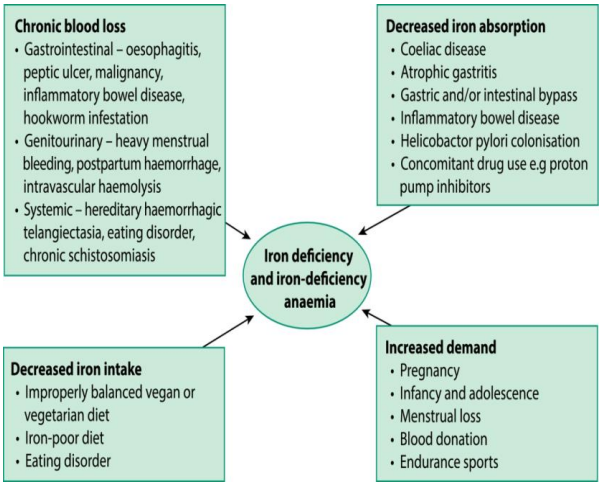

Figure 3 Etiology of Iron deficiency Anemia

Pathophysiology:[17]

Plasma ferritin levels decrease when there is deficiency of iron. Reduction in ferritin level - due to the abnormalities in hemoglobin levels, serum iron level or in erythrocyte size becomes apparent. Elimination of Iron is not controlled physiologically – so homeostasis is maintained by iron absorption. Anemia may result from a mis-match between the body's iron requirements and iron absorption. Demand of iron varies with age.

Daily requirements for iron: Infants - 0.5 mg, Adolescent male - 1.8 mg, Adolescent female - 2.4 mg, Adult male - 0.9 mg, Menstruating female - 2.0 mg, Pregnancy - 3-5 mg , Postmenopausal female - 0.2 mg

Signs and Symptoms : [11]

1. Breathlessness
2. Pale skin and mucous membrane
3. Painless glossitis
4. Angular stomatitis
5. Koilonychia (spoon-shaped nails)
6. Dysphagia (due to pharyngeal web)
7. Pica syndrome (unusual cravings)atrophic gastritis.

Diagnosis: [16] Identified on the basis of medical history, complete blood count, and peripheral smears.

Treatment:

1. Oral iron therapy – Ferrous Sulphate 200 mg, Ferrous Gluconate 300 mg, Ferrous Fumarate 200 mg
2. Parenteral iron therapy – Iron Dextran, Iron Sucrose, Ferric Gluconate

B. Vitamin B_{12} Deficiency Anemia: Vitamin B_{12} is an essential vitamin with largely non vegetarian source. Indian population, with largely vegetarian habit, is more prone to harbour deficiency of vitamin B_{12}.[18,19]

Etiology: [20]

Vitamin B_{12} deficiency has 3 primary etiologies:

1. Autoimmune- Anti-intrinsic factor antibodies bind to and inhibit the effects of intrinsic factor, resulting in an inability of B_{12} to be absorbed by the terminal ileum. Eg. Pernicious anemia.
2. Malabsorption Parietal cells in the stomach produce intrinsic factor; therefore, any patient with a history of gastric bypass surgery may be at risk for developing a B_{12} deficiency because their new alimentary pathway bypasses the site of intrinsic factor production.
3. Dietary Insufficiency- a strict vegan diet for approximately three years may develop a B_{12} deficiency from a lack of dietary intake.

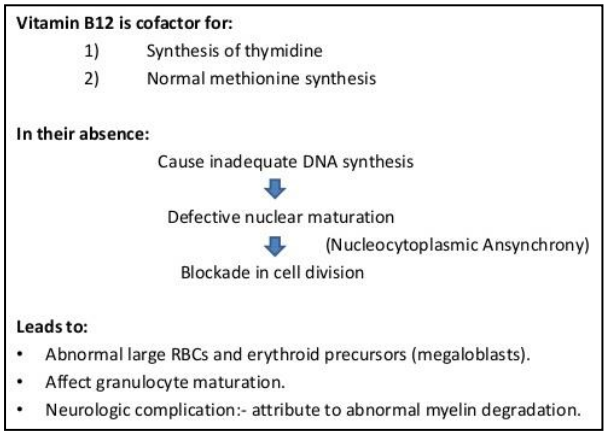

Figure 4 Pathophysiology of vitamin B12 deficiency Anemia

Clinical manifestation: [21]

Cutaneous: Hyperpigmentation, Jaundice, Vitiligo
Gastrointestinal: Glossitis
Hematologic: Megaloblastic, Macrocytic anemia, Leukopenia, Thrombocytopenia, thrombocytosis
Neuropsychiatric: Irritability, Olfactory impairment Peripheral Neuropathy
Diagnosis: [16] A level of less than 150 pg per mL (111pmol per L) is diagnostic for deficiency.
Treatment: [21]

Oral Vitamin B_{12} Therapy - Oral Cyanocobalamin is well absorbed

Parenteral Vitamin B_{12} Therapy - A dose of 1000 mcg of B_{12} via the intramuscular route is recommended once a month. In newly diagnosed patients, 1000 mcg of B_{12} is given intramuscularly once a week for four weeks to replenish stores before switching to once-monthly dosing.

Intranasal Vitamin B_{12} Therapy - an intranasal gel (cyanocobalamin 500 microgram/actuation) is available in United States, with recommended dosing of three times a week.

Complications: [22]

1. Heart failure due to the anemia
2. Severe disabling neurological deficits
3. Risk of gastric cancer
4. Risk of developing an autoimmune disorder like Type 1 Diabetes, Myasthenia Gravis, Hashimoto Disease, or Rheumatoid Arthritis.

C. Folic Acid deficiency Anemia :

Folate is an essential water-soluble vitamin naturally present in food, especially in fruits, green leafy vegetables, and liver. [23,24]

Etiology: [25]

1. Inadequate dietary intake.
2. Over cooking destroys folic acid.
3. Elevated pH, as occurs in Achlorhydria, can also lead to poor folate absorption.
4. Use of drugs such as Methotrexate, Phenytoin, Sulfasalazine and Trimethoprim can antagonize folate utilization, inhibit its absorption or conversion to its active form resulting in folate deficiency.
5. Alcoholism is a significant cause of folate deficiency.
6. Pregnancy, hemolytic anemia, and dialysis can also result in folate deficiency.

Pathophysiology: [23]

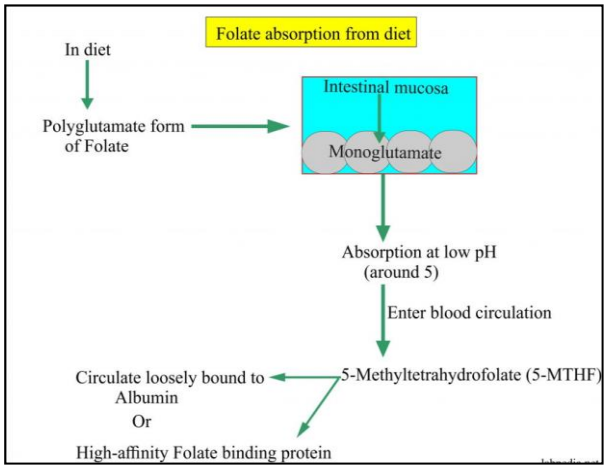

Figure 5 Pathophysiology of Folic acid deficiency Anemia

Signs & Symptoms: [26] The symptoms of folate deficiency are often subtle. They include: Fatigue, Gray hair, Mouth sores, Weakness, Lethargy, Shortness of breath, Tongue swelling, Growth problem, Pale skin, Irritability

Treatment: [16] Oral Folic acid supplementation- 1 mg daily, Parenteral formulation contains 5 mg per mililiter and may be given intramuscularly, subcutaneously, or intravenously.

Diagnosis: Blood test – Check Serum or erythrocyte folate concentration, Increased plasma HCV concentration with normal MMA levels is another indicator of folate deficiency. [16]

REFERENCES

1. WHO, UNICEF. Iron Deficiency Anaemia Assessment, Prevention, and Control A guide for programme managers. 2001. Available at: http://apps.who.int/iris/bitstream/10665/66914/1/W HO_NHD_01.3.pdf. Accessed on 10 May 2017.
2. World Health Organization, Global Nutrition Targets 2025: Anemia Policy Brief, 2014, <https://www.who.int/nutrition/publication/globaltargets2025 policybrief anemia/en/>.
3. World Health Organization, Prevention of Iron Defciency Anemia in Adolescents. Role of Weekly Iron And Folic Acid Supplementation. 2011, <http://www.searo.who.int/entity/child adolescent/documents/sea cah 2/en/>.
4. Kassebaum N, The global burden of anemia. Hematology/ Oncology Clinics of North America 2016; 30: 247–308.
5. Balarajan Y, Ramakrishnan U, Özaltin E, Shankar AH and Subramanian S, Anaemia in low-income and middle-income countries. Lancet 2012; 378: 2123–2135
6. Bharati P, Shome S, Chakrabarty S, Bharati S and Pal M, Burden of anemia and its socioeconomic determinants among adolescent girls in India. Food Nutr Bull 2009; 30: 217–226.
7. Chandrakumari A, Sinha P, Singaravelu S and Jaikumar S, Prevalance of anemia among adolescent girls in a rural area of Tamil nadu, India. Journal of Family Medicine and Primary care 2019; 8 : 1414-1417.
8. Aguayo VM, Paintal K and Singh G, The Aolescent girl's anemia contol programme: a decade of programming experience to break the intergenerational cycle of malnutrition in India. Public Health Nutr**.** 2013;16: 1667-1676.
9. The World Bank, Public health at a glance factsheet, Adolescent Nutrition, 2003.
10. Chaparro C, Suchdev P, Anemia epidemiology, pathophysiology, and etiology in low- and middle- income countries. Annals of the New York Academy of science, 2019; 1450: 15-31.
11. Acomb C. and Holden J. Anemias. In: Walker R. and Whittlesea C editors. Clinical pharmacy and therapeutics. 4th Edn. Churchill Livingstone Elsevier; Edinburgh, 2007; pp 785-799.
12. Badireddy M and Baradhi K. Chronic Anemia StatPearls Publishing; Treasure Island (FL): 2020 May 30.
13. Amin S and Antunes C. Lower Gastrointestinal Bleeding. Pearls Publishing; Treasure Island (FL): 2019 Sep 13.
14. Jamwal M, Sharma P and Das R. Laboratory Approach to Hemolytic Anemia. Indian J Pediatr 2020; 87: 66-74.
15. Mumford J, Flanagan B, Keber B and Lam L, Hematologic Conditions: Platelet Disorders. FP Essent 2019 **;** 485: 32-43.
16. Teresi M. Iron deficiency and Megaloblastic Anemias. In Herfindal ET and Gourley DR Gilman's The Pharmacological Basis of Therapeutics; 6th edn; MacMillan publishing Co. Inc. New York, 1975; pp.1318-1823.
17. Luciana R and Nadya C, Iron deficiency anemia in adolescents; a literature review, Nutricion Hospitalaria, Grupo Aula Medica 2014; 29: 1240-1249.
18. Vitamin B12 Deficiency | National Health Portal of India. Available from: https://www.nhp.gov.in/disease/blood-lymphatic/vitamin-b12-deficiency. Fab 2016
19. Sasidharan PK. B12 deficiency in India. Arch Med Health Sci 2017; 5: 261.
20. Devi A, Rush E, Harper M and Venn B. Vitamin B12 Status of Various Ethnic Groups Living in New Zealand: An Analysis of the Adult Nutrition Survey 2008/2009. Nutrients. 2018**;** 10.
21. Langan R. and Goodbred A J, Vitamin B12 deficiency Recognition and Management. Family Medicine Residency Program, Bethlehem, Pennsylvania **2017,** 96, 384-389.
22. Ziegler O, Sirveaux MA, Brunaud L, Reibel N and Quilliot D, Medical follow up after bariatric surgery: nutritional and drug issues. General recommendations for the prevention and treatment of nutritional deficiencies. Diabetes Metab. 2009; 35: 544-57.
23. Green R and Datta Mitra A, Megaloblastic Anemias: Nutritional and Other Causes. Med. Clin. North Am. 2017**;** 101: 297-317.
24. Attia AAA, Amer MAEM, Hassan M and Din SFG. Low serum folic acid can be a potential independent risk factor for erectile dysfunction: a prospective case-control study. Int Urol Nephrol. 2019 **;** 51: 223-229.
25. Lever EG, Elwes RD, Williams A and Reynolds EH. Subacute combined degeneration of the cord due to folate deficiency: response to methyl folate treatment. J. Neurol. Neurosurg. Psychiatry. 1986 ; 49: 1203-1207.
26. Elaine K L, Folate deficiency: Causes, Symptoms, and Diagnosis https://www.healthline.com/health/folate-deficiency# symptoms. August 2020.